REMARKS

With entry of this amendment, claims 25-29, 39, 44, 47, 51-54, 58 and 59 are pending. Claims 1-24, 30-37, 40-42, 48-50 and 55-57 were withdrawn and have been canceled without prejudice. Claims 45 and 46 have also been canceled without prejudice. Applicants reserve their right to prosecute subject matter of the canceled claims in subsequent applications.

Claims 25, 44, 47, 52 and 53 have been amended to delete recitation of "or substantially similar" and to delete non-elected nucleic acid sequences. Also, these claims have been amended to recite the identical sequence or at least 98% sequence similarity and encoding a polypeptide having 3'-5' exonuclease activity of SEQ ID NO:23. Support for these amendments is in the specification on page 20, line 14-page 21, line 11.

Claims 27 and 28 have been amended to correct antecedent basis by correcting claim dependency.

Claims 38 and 39 have been amended to clarify that the claims recite a transgenic plant or progeny thereof, or seeds thereof comprising the plant cell of claim 25 or 26, respectfully.

Claim 43 has been canceled and claim 44 has been amended to be independent.

Claim 46 has been canceled and claim 47 has been amended to be independent.

Claims 43, 47 and 53 have been amended to delete recitation of altering or reducing expression of SEQ ID NO:24 by homologous recombination or chimeric oligonucleotides.

Claim 51 has been amended to more specifically point out and distinctly claim the present invention by reciting a method for stabilizing the expression of an exogenous nucleotide sequence of interest in a transgenic plant cell or plant comprising the steps of:

a) obtaining a transgenic plant cell or plant having altered expression of an endogenous nucleotide sequence of said plant cell or plant comprising a first expression cassette that encodes a polypeptide comprising a 3'-5' exonuclease domain, and wherein said polypeptide is identical to an amino acid sequence of SEQ ID NO:24; and

b) introducing into said transgenic plant cell or plant an exogenous nucleotide sequence of interest,

wherein the expression of said exogenous nucleotide sequence of interest in said transgenic plant cell is stabilized as compared to the expression of said nucleotide sequence of interest in a plant cell or plant lacking said first expression cassette and to provide antecedent basis for the phrase "a first expression cassette." Support for these amendments is in the specification on page 13, lines 1-13.

Claim 54 has been amended to recite the method according to claim 53, wherein the expression of said endogenous nucleotide sequence is reduced by deleting the phrase "in a plant cell" and correcting its dependency.

Claims 44, 47 and 53 have been amended to recite a methods of altering the expression of a gene of interest by modifying by insertional mutagenesis in said plant cell at least one chromosomal copy of the nucleotide sequence identical or having at least 98% sequence similarity and encoding a polypeptide having 3'-5' exonuclease activity to SEQ ID NO:23 or of a regulatory region thereof. Support for these amendments is on page 31, lines 4-16.

No new matter has been added by these amendments.

Specification

The substitute specification has not been entered because it does not conform to 37 CFR 1.125(b) because the statement as to a lack of new matter is missing. However, the substitute specification would be objected to for containing new matter (new sequences).

Please do not enter the substitute specification.

Sequence Listing

The CRF of the original sequence listing was found to have errors and the substitute specification was found to contain new sequences. Applicants are requested to submit a corrected sequence listing without the additional sequences.

In response, Applications submit a corrected original sequence listing.

Applicants hereby provide a Computer Readable Form of the Corrected Sequence Listing as well as the Paper Copy thereof. The undersigned states that the Paper Copy and the Computer Readable Form, submitted in accordance with 37 CFR §1.821(c) and (e), respectively, are the same. No new matter has been added.

Claim Objections

Renumbered claims 58 and 59 are objected to because of informalities. In line 1 of both claims the article "A" should be "the". The claims have been amended to correct this informality.

Claim Rejections under 35 USC 101

Claims 25-29, 38, 39, 58 and 59 are rejected under 35 USC 101 because the claimed invention is allegedly directed to non-statutory subject matter since the claims are drawn to any plant cell or plants have the same characteristics as those found naturally. It is suggested that the claims be amended by inserting language that identifies products that cannot be found in nature.

In response, these claims have been amended to recite "transgenic" plant cells or plants. These amendments overcome this rejection and Applicants request its withdrawal.

Claim Rejections 35 USC 112, second paragraph

Claims 25-29, 38, 39, 43-47, 51-54, 58 and 59 are rejected under 35 USC 112, second paragraph, for allegedly being indefinite.

Claims 25, 43-47, 51-53 are rejected by the recitation of the phrase "substantially similar".

Claim 27 is rejected for recitation of the phrase "the insertion of a nucleic acid molecule comprises one T-DNA boarder region" for lacking antecedent basis.

Claim 28 is rejected for reciting "the insertion comprises a transposable element" for insufficient antecedent basis.

Claims 38 and 39 are rejected as being unclear if the progeny and seeds also comprises the plant cell of claim 25.

Claim 43 is rejected for not reciting positive steps.

Claims 44, 47 and 53 are rejected for recitation "chromosomal copy of the nucleotide sequence identical to . . ." SEQ ID NO:23 because it is a cDNA and not present in chromosomes.

Claim 45 is rejected for the recitation of "a means" is unclear.

Claim 46 is indefinite because it is not clear how the expression of the nucleotide sequence is being altered. It is considered unclear how one defines the alteration of expression of the introduced sequence versus a non-altered expression.

Claim 51 is indefinite for the recitation "Stabilizing the expression" in line 1 and "stabilized" in line 11. It is allegedly not clear if the method is for the expression of nucleotide sequences whose expression does not need to be stabilized. It is considered unclear what is considered stable versus unstable expression.

Claim 51 the recitation of "in a plant cell of an endogenous nucleotide sequence of said plant cell or plant that encodes a polynucleotide" is considered unclear.

Claim 51 the recitation of "said first expression cassette" has insufficient antecedent basis.

Claim 54 the recitation "in a plant cell" in allegedly unclear if the plant cell is the same plant cell mentioned in the claims from which 54 depends. It is suggested to delete this recitation.

In response, the claims have been amended to more particularly point out and distinctly claim the invention and these amendments overcome these rejections.

Claim Rejections under 35 USC 112, first paragraph

Claims 25-29, 38, 39, 43-47, 51-54 58 and 59 are rejected under 35 USC 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention. In particular, the Office Action alleges that the specification does not describe any sequences that are "substantially similar" to SEQ ID NO:23 or that encode the polypeptide of SEQ ID NO:24 or regulatory region thereof.

The legal standard for meeting the written description requirement under section 112, first paragraph, is whether "the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar,* 935 F.2d 1555, 1563-64, 19 USPQ2d 1111,1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed.

In response, the phrase "substantially similar" has been deleted from the claims. The claims have been amended to recite a sequence having at least 98% sequence similarity and encoding a protein having 3'-5' exonuclease activity. SEQ ID NO:23 has been found to be 97% similar in sequence with wrnexo from *Arabidopsis*, as discussed in the specification.

Applicants also respectfully disagree with the statement that the specification does not teach a mutant. The insertional mutant described in Example 2 on pages 48-49 of the specification. The T-DNA insertions was 26 bp 5' of the predicted CDS region of SEQ ID NO:1. Thus, at least one mutant was described.

Claim Rejections under 35 USC 112, first paragraph

Claims 25-29, 38, 39, 43-47, 51-54, 58 and 59 are rejected under 35 USC 112, first paragraph, as allegedin containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, to make and use the invention.

Enablement of a disclosure "is not precluded by the necessity for some experimentation such as routine screening." In re Wands, 858 F.2d 731, 736-7 (Fed. Cir. 1988) (citations omitted). The experimentation necessary must not be undue. Id. At 737. Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. Fields v. Conover, 170 USPQ 276, 279 (CCPA 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been listed in Wands, 858 F.2d at 737. Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine. Id.

The relevant inquiry for determining whether the scope of the claims is commensurate with the specification is "whether the scope of enablement provided to one of ordinary skill in the art by the disclosure is such as to be commensurate with the scope of protection sought by the claims." In re Moore, 439 F.2d 1232, 1236 (CCPA 1971) (emphasis added). "A patent need not teach, and

preferably omits, what is well known in the art." Hybridtech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986), cet. Denied, 480 U.S. 947 (1987).

While predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of the experiment is not a consideration. Indeed, the Court of Customs and Patent Appeals has specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue (see In re Angstadt, 190 USPQ 214 (CCPA 1976)).

In response, Attorneys for Applicants respectfully point out that the claims have been amended to delete recitation of the phrase "substantially similar" and has been replaced with the phrase "having at least 98% sequence similarity and encoding a polypeptide having 3'-5' exonuclease activity. The gene has been confirmed to encode a protein having 3'-5' exonuclease activity and can digest RNA when expressed in *E. coli*. (data not shown).

Applicants respectfully point out that due to the redundancy of the genetic code, one skilled in the art would easily be able to create nucleotide molecules that encode the polypeptide of SEQ ID NO:24 that differ from the nucleotide sequence of SEQ ID NO:23 but still encode the same protein.

Regarding the rejections relating to methods using homologous recombination or chimeric polynucleotides, the claims have been amended to delete these methods, thus making these rejections moot.

Regarding the rejection on page 14 of the Office Action that alleges "the specification does not teach what the effect on a plant would be in which the expression of the endogenous nucleotide sequence was reduced", Applicants have the following comments.

The specification as filed indeed describes and teaches the effect on a plant when the expression of the endogenous nucleotide WEX sequence is reduced. The specification teaches in Example 5, that when Post-transcriptional gene silencing (PTGS) is blocked in the RDRD deficient homozygous mutant, the plant PTGS of the 35S-GFP reporter gene is lost in plants having the T-DNA insert in SEQ ID NO:23 (also called the WEX gene (the mutant is termed wex-1). Further, in Example 9, the complementation experiments show that expression of RFRF is required for PTGS. Therefore, the specification does describe and teach the phenotype when the plant have decreased expression of SEQ ID NO:23. Additionally, the attached manuscript entitled "A Gene Encoding an RNase D Exonuclease-Like Protein is Required for Posttranscriptional Silencing in *Arabidopsis*" (exhibit A) describes further experiments conducted on SEQ ID NO:23 now called WEX.

Regarding the overall effect on the plant, it has recently been discuvered that the expression of certain microRNAs is reduced in the RDRD mutant. This is direct evidence for effects on silencing of endogenous genes. MicroRNAs are silencing-related small RNAs encoded by

endogenous genes and are believed to have an important regulatory function in plants and animals. If the examiner wishes to see this data, Applicants can supply it.

Regarding the observation that Transcriptional gene silencing is not affected, the Applicants note that they have data that TGS is not affected in the mutant (see manuscript).

Regarding the manner in which the claimed methods would alter expression, on page 15 of the Office Action, it alleges the only manner the claimed methods would alter expression is by increasing expression of a gene of interest. Suppression of the expression of the endogenous SEQ ID NO:24 would result in a loss of PTGS and an increase in expression of the nucleotide sequence of interest. Thus, the claimed methods increase or "stabilize" the expression of a nucleotide sequence of interest by preventing suppression by PTGS, as compared to the parent plant that expresses the exonuclease.

Claim Rejections under 35 USC 102

Claims 25, 29 and 59 are rejected under 35 USC 102(b) as being allegedly anticipated by Elmayan et al. (Plant Cell, 1998, 10:1747-1757) in light of Suzuki et al. (An introduction to Genetic Analysis, 4th Edition. Elmayan allegedly teaches *Arabidopsis* plants mutagenized with EMS in which the plants show decreased levels of PTGS and the mutated endogenous sequence in the plant cells is substantially similar to SEQ ID NO:23. The instant specification allegedly does not clearly define "substantially similar" and it is inherent that the EMS treatment caused a point mutation as taught by Suzuki.

The legal test for anticipation under 35 U.S.C. § 102 requires that each and every element of the claimed invention be disclosed in a prior art reference in a manner sufficient to enable one skilled in the art to reduce the invention to practice, thus placing the public in possession of the invention. W.L. Gore Assoc. v. Garlock, Inc., 721 F.2d 1540, 1554 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1994); In re Donohue, 766 F.2d 531 (Fed. Cir. 1985). Anticipation under 35 U.S.C. § 102 requires identity of invention. Scripps Clinical & Research Fdn. v. Genentech, Inc., 927 F.2d 1565 (Fed. Cir. 1991).

The claims as amended recite to transgenic plant cells comprising the recite sequence. Elmayan does not describe transgenic plant cells or plants comprising the nucleic acid molecule of SEQ ID NO:23. Therefore, Elmayan does not anticipate the present invention.

Conclusion

The above remarks and amendments put the present application in form for allowance, and Application respectfully request such action.

Respectfully submitted,

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